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Familial drusen associated with choroid neovascularization and its diagnostic and therapeutic challenges

Drusas familiares associadas à neovascularização coroideana e os desafios diagnóstico e terapêutico

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KEYWORDS:

Doyne macular dystrophy; Malattia leventinese; Retinal drusen.

ABSTRACT

Malattia leventinese or Doyne macular dystrophy is a rare autosomal dominant disease caused by a mutation in *EFEMP1*. It is characterized by the presence of numerous drusen with radial distribution at the posterior pole. Herein we present the case of a 39-year-old patient who underwent ophthalmological consultation and complained of low visual acuity in the left eye since approximately 2 years before. The diagnostic hypothesis of malattia leventinese with choroid neovascularization in the left eye was suggested after clinical evaluation and complementary investigation.

PALAVRAS-CHAVE:

Distrofia macular de Doyne; *Malattia Leventinese*; Drusas retinianas.

RESUMO

A m*alattia leventinese* ou distrofia macular de Doyne é uma doença autossômica dominante rara, causada por uma mutação no gene EFEMP1, caracterizada pela presença de inúmeras drusas com distribuição radial no polo posterior. Trata-se de uma paciente de 39 anos de idade que apresentou, à consulta oftalmológica, queixa de baixa acuidade visual no olho esquerdo (OE) percebida há aproximadamente dois anos. Foi aventada a hipótese diagnóstica de m*alattia leventinese* com neovascularização de coroide no olho esquerdo, após avaliação clínica e propedêutica complementar.

INTRODUCTION

Malattia leventinese (ML) is a rare autosomal dominant retinal dystrophy that was first described in Switzerland in 1925[1]. It is a macular disease characterized by the presence of amorphous deposits, known as drusen, between the retinal pigment epithelium (RPE) and Bruch's membrane. Drusen can appear in a mosaic pattern, which is why the disease is also named honeycomb dystrophy or Doyne dystrophy[2,3].

The great importance of this disease is related to the fact that the main clinical alteration, i.e., drusen, is also a striking characteristic of other retinal dystrophies and age-related macular degeneration (ARMD)[4,5].

The formation of subretinal neovascular membrane (SRNVM) is an unusual but threatening complication of ML, as it can result in irreversible visual damage and legal blindness in young adults[6,7]. The treatment of complications associated with SRNVM should be carefully analyzed, as a conservative approach is invariably associated with a worse prognosis[7,8].

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CASE REPORT

A 39-year-old female patient underwent an ophthalmological consultation owing to the complaint of low visual acuity (LVA) in her left eye (OS).

She reported regular treatment for hypothyroidism, but denied any family history of blindness or LVA.

On ophthalmological examination, best corrected visual acuity of 20/25 in the right eye (OD) and finger counting at 20 cm in the OS were observed. Biomicroscopic examination of the anterior segment and Goldmann applanation tonometry revealed normal findings in both eyes (OU). Indirect binocular ophthalmoscopy of the OD revealed multiple yellowish-white lesions of varying sizes, consistent with macular drusen, particularly in the temporal direction from the fovea; in the OS, in addition to the presence of diffuse drusen, there was retinal thickening secondary to scar tissue formation, possibly due to SRNVM formation (Figure 1).

In view of the clinical findings, she underwent a complementary diagnostic investigation for better evaluation. Fluorescein angiography revealed several

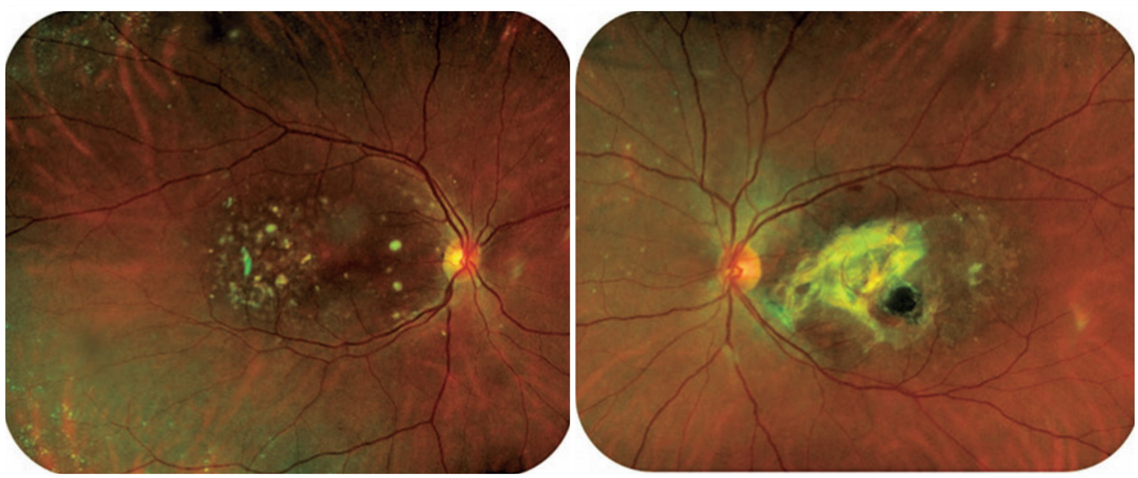


Figure 1. Retinography of the right eye revealing multiple yellowish-white lesions of varying sizes, particularly in the temporal direction from the fovea. In the left eye, diffuse drusen and retinal thickening secondary to scar tissue formation can be observed, possibly resulting from a subretinal neovascular membrane.

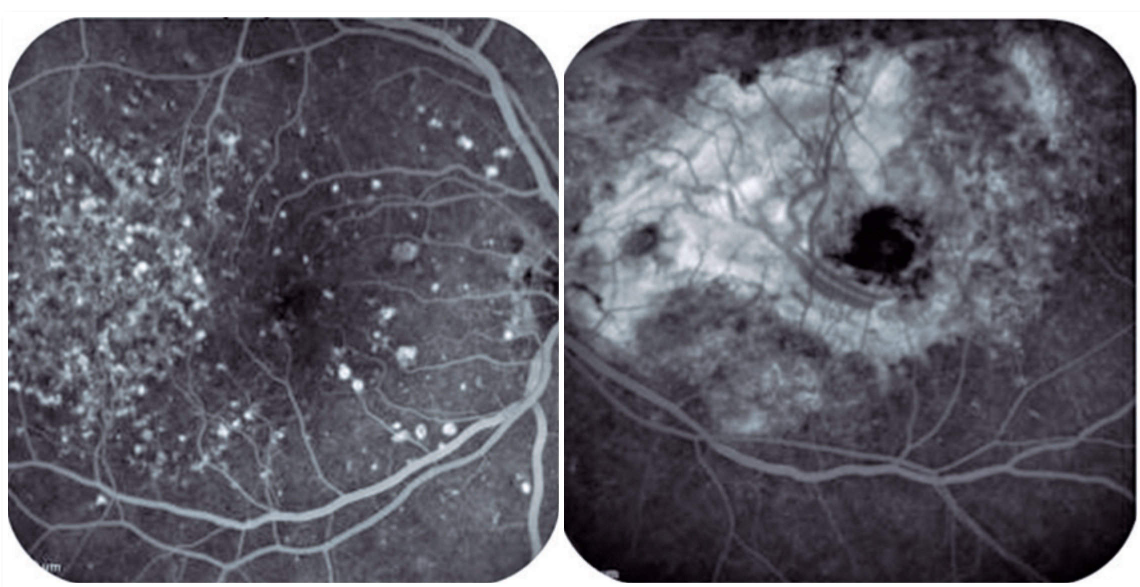


Figure 2. Fluorescein angiography showing several spots of hyperfluorescence affecting the entire region of the macula of the right eye owing to contrast impregnation in the drusen, and an extensive area of hyperfluorescence with contrast tissue impregnation in the macular region of the left eye, consistent with a disc-shaped scar secondary to a subretinal neovascular membrane.

hyperfluorescent spots affecting the entire macular region of the OD due to contrast impregnation in the drusen, and an extensive area of hyperfluorescence with contrast tissue impregnation in the macular region of the OS, consistent with a disc-shaped scar secondary to SRNVM (Figure 2). Autofluorescence examination revealed hyperautofluorescent spots in the macular region of the OD and a hypoautofluorescent area indicating retinal atrophy in the macular region of the OS (Figure 3). Full-field electroretinogram was inconclusive, and electro-oculogram presented macular and cone functional impairment in OU. Optical coherence tomography (OCT) revealed focal, hyper-reflective, subepithelial lesions suggestive of drusen in the macular region of the OD. In the OS, OCT revealed an extensive hyper-reflective area associated with disorganization of the retinal layer microarchitecture, suggestive of fibrotic scar tissue (Figure 4). Further, OCT showed no changes in the optic disc.

In view of the clinical changes and complementary tests, the diagnostic hypothesis of ML was suggested. However, diagnostic confirmation via genetic testing has not yet been obtained.

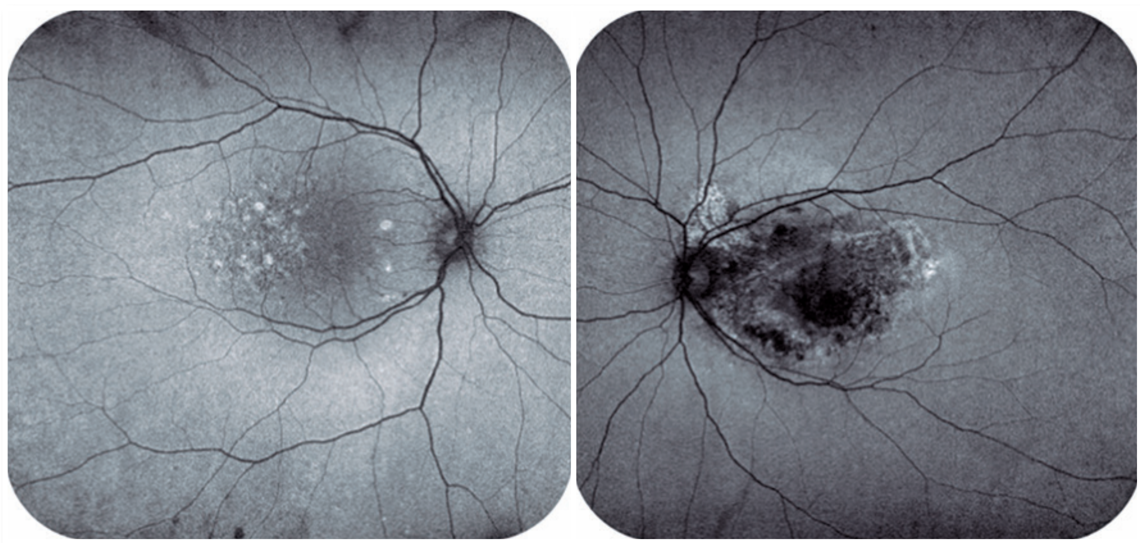


Figure 3. Autofluorescence examination showing hyperautofluorescent spots in the macular region of the right eye and a hypoautofluorescent area indicating retinal atrophy in the macular region of the left eye.

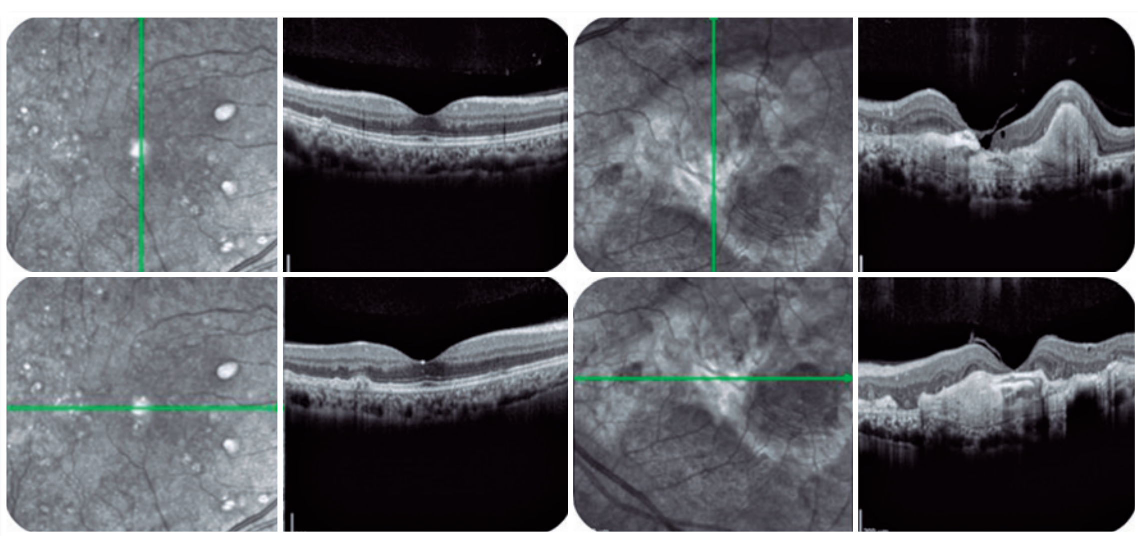


Figure 4. Optical coherence tomography showing focal, hyper-reflective subepithelial lesions suggestive of drusen in the macular region of the right eye, and an extensive hyper-reflective area associated with disorganization of the retinal layer microarchitecture, corresponding to fibrotic scar tissue, in the left eye.

DISCUSSION

ML is a rare, hereditary, degenerative macular disease characterized by the presence of drusen in a characteristic pattern, which may aid in the diagnostic suspicion of this disease[9,10]. ML has no pathognomonic characteristics, but its differentiation from other macular disorders is important because the exact diagnosis may have implications involving genetic counseling and therapeutic strategies.

Studies have identified *EFEMP1* as the responsible gene[4], which enables the diagnostic confirmation of ML via genetic testing. Despite the unavailability of genetic testing data in the presently reported case, the significant clinical changes evidenced in ophthalmoscopy and the emergence of multiple drusen at an early age and arranged in a peculiar pattern enabled the presumed diagnosis of ML.

The differential diagnosis of ML involves a heterogeneous group of retinal diseases in which macular drusen occur. These diseases are characterized by different modes of inheritance, age at onset, electrophysiological findings, and degree of visual disability[5,6]. One of these diseases is ARMD, a chronic and progressive retinal disease that may be associated with irreversible central vision impairment in the elderly population[4]. If ML results in extensive changes in the RPE, then geographic atrophy and SRNVM may be risk factors for legal blindness in the younger, economically active population[6].

In the presently reported case, the patient already had a disc-shaped scar in the OS, possibly secondary to previous choroid neovascularization (with no signs of activity upon admission). Therefore, only conservative treatment was indicated.

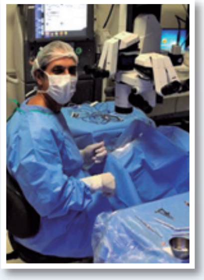
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